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Social Neuroscience:

How a Multidisciplinary Field Is Uncovering the Biology of Human Interactions

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Editor's note: Studying only the biological or social aspects of a species can cause researchers to overlook many of the complex elements at work within and among organisms. The interdisciplinary field of social neuroscience serves to close the gaps left by such singularly focused research. Social neuroscientists boost our knowledge of the biology of animal and human interactions in areas as diverse as drug abuse, pair-bonding, and social isolation. As the field continues to grow, we will better understand the social, biological, and cognitive factors that determine how we relate to others.

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Aristotle observed that we are fundamentally a social species.[1] Social species create emergent structures beyond the individual, ranging from dyads (or pairs) and families to groups, communities, and cultures. What Aristotle did not appreciate is that these emergent structures evolved hand in hand with the neural, neuroendocrine, cellular, and genetic mechanisms that support them. Evolving social behaviors helped these organisms survive, reproduce, and care for dependent offspring for a sufficiently long time that they too reproduced.

Not long ago, scientists thought that social factors were relatively unimportant to the basic structure and function of the brain and biology because of their relatively recent emergence in species. The social brain hypothesis, however, posits that the social complexities of primate species contributed to the rapid increase in neocortical connectivity and intelligence.[2] Deducing better ways to find food, to avoid perils, and to navigate territories has adaptive value for large mammals, but the complexities of these ecological demands are no match for the complexities of social living. Communal living requires learning by social observation; recognizing the shifting status of friends and foes; anticipating and coordinating efforts among individuals; using language to communicate, to reason, to teach, and to deceive others; orchestrating relationships; navigating complex social hierarchies, social norms, and cultural developments; subjugating self-interests for the interests of the pair bond or social group in exchange for the possibility of long-term benefits; recruiting support to sanction individuals who violate group norms; and accomplishing all these tasks across time frames that draw on lessons learned from the distant past to mental simulations of multiple possible futures.[2] Consistent with this hypothesis, researchers found a composite index of sociality in troops of baboons to be highly correlated with infant survival, and they have shown through cross-species comparisons that the evolution of large and metabolically expensive brains is more closely associated with social complexity than ecological complexity.[2]

Over the past two decades, social neuroscience emerged as a field dedicated to investigating the social brain. Scientists, ranging from physicists to psychologists, epidemiologists to neurologists, philosophers to neurobiologists, and entomologists to zoologists, have begun working together in interdisciplinary scientific teams using animal models, patient studies, and research on normal individuals to investigate the biological mechanisms underlying social interactions—described by neuroscientists Christopher Frith and Daniel Wolpert as one of the major problems for the neurosciences to address in the 21st century.[3] The convergence of

these diverse methodologies is advancing our understanding of the mechanisms underlying complex social behavior. Large interdisciplinary teams are now the rule rather than the exception in social neuroscience. Indeed, the obstacles of geographic as well as disciplinary boundaries among scientists are diminishing.

Twenty years after its beginnings at Ohio State University, social neuroscience is now an active area of research across the globe, fueled by the establishment of societies and journals to advance scientific research, education, and clinical applications. Among the questions that social neuroscientists are actively investigating are the effects of social factors on brain and biological functioning; the supposed existence of specialized circuits for social functions; the nature of interdependencies between genes and social environments; and the biological mechanisms underlying social cognition and emotions, social connections, social interactions, and group processes.

In recent years, social neuroscientists have shed light on the beneficial role of social connections for the brain and the body. Epidemiological research, for example, indicates that social isolation predicts morbidity and mortality.[4] The initial explanation for this finding was that family and friends promote positive health behaviors in individuals, and socially isolated individuals are more likely to display poor health behaviors and, consequently, fall victim to morbidity and early mortality. Longitudinal studies in humans have called this explanation into question, however, and experimental studies in nonhuman social species show that isolated animals also incur earlier morbidity and mortality. We will return later to the deleterious cognitive and biological effects of isolation in social species.

The compelling need to integrate biology and the social sciences is also apparent when considering the effects of the social environment on health and mortality. Researchers have found that, in addition to social isolation, factors like socioeconomic status,[5] household income disparities,[6] social networks,[7] and neighborhood crime[8] strongly influence morbidity and mortality. The Whitehall Studies, which focus on the long-term health of civil servants, have demonstrated the so-called social gradient—a direct association between socioeconomic status and health outcomes across the life span, which is explained in part by compromised immune functioning in individuals who are lower in social position.[5, 9]

Principles of Social Neuroscience

The first principle, multiple determinism, specifies that a social behavior at one level of organization (for example, attachment at the dyadic level) can have multiple antecedents within or across levels of organization (for example, various hormonal influences on attachment).[10] On a biological level, researchers identified the contribution of individual differences in the endogenous opioid receptor system (a system produced by the body that has opiate-like effects, such as the painkilling properties of endorphins) in drug use, a discovery that may help illuminate the neural mechanisms underlying addiction. On a social level, investigators noted the important role of social context (e.g., the extent to which a social animal is isolated) in impulsive and addictive behaviors, a finding that may help us identify situational triggers.[11] Because the social context interacts with individual differences at the level of receptors in the brain, our understanding of drug abuse is incomplete if either level is excluded. More generally, the principle of multiple determinism means that we are unlikely to achieve a complete understanding of social behavior if we limit analyses to any single level of organization.

As another example, researchers once thought that immune functions simply reflected physiological responses to pathogens or tissue damage. It is now clear that immune responses are influenced by central nervous processes, which, in turn, are affected by interpersonal interactions. Researchers have shown that adverse social interactions alter immune function through their effects on neuroendocrine activity.[12] An understanding of human immune responses in everyday life is inadequate in the absence of consideration of social and behavioral factors. Comprehensive behavior theories thus require understanding of biological, social, and other factors. Accordingly, neuroscientists and the social scientists will advance their respective fields by increasing their scope of analysis to include factors and processes from both perspectives.

The second principle, nonadditive determinism, specifies that properties of the whole are not always readily predictable by the simple sum of their parts. Consider a study of the effects of amphetamine. Researchers examined the behavior of nonhuman primates following the administration of amphetamine or placebo. No clear pattern emerged between the drug and placebo conditions until researchers considered each primate's position in the social hierarchy. Amphetamine was found to increase dominant behavior in primates high in the social hierarchy and to increase submissive behavior in primates low in the social hierarchy.[13] A strictly

physiological or social analysis, regardless of the sophistication of the measurement technology, would not have revealed the orderly relationship between amphetamine use and behavior.

The third principle, reciprocal determinism, specifies that there can be mutual influences among biological and social factors in determining behavior. Researchers not only have shown that the level of testosterone in nonhuman male primates promotes sexual behavior, but also have found that the availability of receptive females influences the level of testosterone in males. This principle implies that scientists cannot craft comprehensive accounts of behavior if they consider the biological or the social level of organization unnecessary or irrelevant.

In sum, social neuroscience flourishes in part because of the increasingly sophisticated techniques for mapping the functional anatomy of the brain, neural circuits, endocrine systems, and cellular and molecular processes. But the field also flourishes because of its unique perspective. If the solitary computer is a metaphor for cognitive neuroscience, the Internet is a metaphor for social neuroscience. For instance, cognitive neuroscientists see language as a symbol system that promotes the abstraction and manipulation of environmental information. Social neuroscientists see language as a communication system that promotes interaction, coordination, and problem solving. Both perspectives can produce valuable insights into the functions of neural structures and processes, but the functions that each perspective reveals are different.

Further Integration Within Social Neuroscience

Humans are a unique social species in that our social institutions, civilizations, and cultures are highly developed; our territorial reach knows few boundaries; and our selection of and impact on the environment in which we live—and the impact of this environment on our genes—are unmatched. Despite these differences, we share much in common with other social species. Social neuroscience investigations reflect two largely separate root systems: one based on data from humans and grounded in the discipline of psychology, and the other based on data from animal models and grounded in biology and biomedicine.

With a few notable exceptions, there was only modest communication between these two groups of scientists in the early years of social neuroscience.[14] With the emergence of the international, interdisciplinary Society for Social Neuroscience in 2010, this gap is being filled. It is important that those primarily interested in explaining human behavior begin to validate their

hypotheses using animal models, including the study of the behavioral impact of pharmacological modulations and brain lesions that closely mimic some of the lesions found in humans. It is also important for those primarily using animal models to understand the psychological constructs used by scientists studying human mental and behavioral processes. This will allow the former to better develop appropriate behavioral paradigms. By bridging the gap between animal and human studies, social neuroscience contributes much to our understanding of the mechanisms by which the social world (and its disorders) impacts health, life span, and cognition.

A growing body of interdisciplinary studies shows that social interaction and pair-bonding may have a profound effect on health and cognition, in both animals and humans.[15] In addition, empirical evidence involving autonomic, endocrine, and immune functioning suggests that the physiological effects of social isolation and loneliness unfold over a relatively long time period and may predict morbidity and mortality from cancer and cardiovascular disease.[16] These interdisciplinary findings highlight the complex role of social interactions and their effects on health, biology, brain, and cognition.

Moreover, interdisciplinary investigations of the commonalities and differences *across* social species (and across cultures within social species) are becoming increasingly important. When researchers found a concentration of oxytocin and vasopressin receptors (pituitary hormones) in dopamine-rich areas of the brain in the monogamous prairie vole, our understanding of social bonds advanced. Researchers found a concentration of these receptors at sites distal to regions associated with reward and reinforcement in the more solitary montane and meadow voles.[15] These findings highlight the crucial relationship between pituitary hormones and both pair-bonding and social behaviors. Related work further suggests that polymorphisms in oxytocin receptors are involved in the sociality of voles, birds, and humans, which, in turn, suggests that significant evolutionary changes in social behavior may occur through variation in regulatory regions of genes already involved in social behavior.[17] Further, animal research has led to experimental studies in humans contrasting the effects of oxytocin nose sprays versus placebo in order to better understand the modulator role of this peptide hormone on social interactions, pair-bonding, and trust.

The Case of Social Isolation

Animal models significantly inform human studies, and vice versa. In a large prospective study, Robert S. Wilson and his colleagues at the Rush Alzheimer's Disease Center assessed 823 older adults free of dementia at enrollment. Participants completed an extensive battery of cognitive measures to assess global cognition, episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability. The greater the perceived social isolation of the participants, the poorer their cognitive performance within each of these domains at baseline. In addition, loneliness was associated with greater cognitive declines in every domain except working memory and episodic performance. Furthermore, 76 individuals developed dementia during the 65-month study period. Models that controlled for age, sex, and education indicated that loneliness significantly increased the risk of developing clinical Alzheimer's disease, and this association was unchanged when objective social isolation and other demographic and health-related factors served as covariates. The fact that subjective rather than objective social isolation predicted cognitive decline means that the brain played a central role.[18]

Further evidence for the causal role of social isolation comes from experimental studies in nonhuman social species. For instance, Zachary Weil and his colleagues at Ohio State University investigated inflammatory responses in the brain and neuronal death in isolated versus nonisolated mice following cardiac arrest and cardiopulmonary resuscitation. The experimental manipulation of social isolation caused greater neuroinflammation and greater brain-cell loss.[19] The extent to which neuroinflammation in humans is responsible for the association between isolation and cognitive decline is an important question raised by these studies.

Additional deleterious effects of experimentally manipulated social isolation are decreases in the lifespan of the fruit fly,[20] increases in mortality rates following experimentally induced stroke in mice,[21] increases in obesity and diabetes rates in mice,[22] increases in the growth of cancerous tumors in rats,[23] increases in stress hormone levels and oxidative stress in rabbits,[24] and an elevated morning rise in cortisol in squirrel monkeys.[25]

The effects of isolation in humans have much in common with the effects of isolation found in nonhuman social species. Researchers found increased activation of the brain's stress systems, vascular resistance, and blood pressure, as well as decreased inflammatory control, immunity, sleep salubrity, and expression of genes regulating glucocorticoid responses and

oxidative stress.[26] In sum, the health, life, and genetic legacy of members of most social species are threatened when they find themselves on the social perimeter.

The Future of the Field

Social neuroscience opens a critical avenue for a better understanding of the biology of connected minds. Now that researchers have articulated the conceptual framework and main principles of social neuroscience, the most immediate challenge is to translate more widely the findings from the laboratory to society. A multilevel integration of the social, biological, and cognitive factors known to determine behavior could provide scientists and practitioners with new therapeutic interventions to address acute and chronic individual, communicative, and social disorders such as autism, psychopathy, and social phobias.

The road ahead is replete with conceptual challenges and methodological issues, but it also promises exciting scientific discovery. The recent emergence of scientific journals, handbooks, and societies in social neuroscience is symbolic of productive interdisciplinary dialogues linking traditional biological and behavioral analyses with more contemporary approaches, including neuroimaging and genomics. Finally, the appeal of the big questions addressed by social neuroscience to young interdisciplinary investigators suggests a bright future for this field as researchers continue transforming social neuroscience research into mainstream science.

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References

1. Aristotle. (1984). *The politics* (C. Lord, Trans.). Chicago: University of Chicago Press.

2. Dunbar, R. I., & Shultz, S. (2007). Evolution in the social brain. *Science, 317*(5843), 1344-1347.

3. Frith, C. D., & Wolpert, D. M. (2004). *The neuroscience of social interaction: Decoding, imitating, and influencing the actions of others*. New York: Oxford University Press.

4. House, J. S., Landis, K. R., & Umberson, D. (1988). Social relationships and health. *Science, 241*(4865), 540-545.

5. Marmot, M. G., & Wilkinson, R. G. (2006). *Social determinants of health* (2nd ed.). New York: Oxford University Press.

6. Wilkinson, R. G., & Pickett, K. (2010). *The spirit level: Why greater equality makes societies stronger*. New York: Bloomsbury Press.

7. Christakis, N. A., & Fowler, J. H. (2009). *Connected: The surprising power of our social networks and how they shape our lives* (1st ed.). New York: Little, Brown and Co.

8. Sampson, R. J. (2003). The neighborhood context of well-being. *Perspectives in Biology and Medicine, 46*(3 Suppl), S53-64.

9. Marmot, M. G., Smith, G. D., Stansfeld, S., Patel, C., North, F., Head, J., . . . Feeney, A. (1991). Health inequalities among British civil servants: The Whitehall II study. *Lancet, 337*(8754), 1387-1393.

10. Cacioppo, J. T., & Berntson, G. G. (1992). Social psychological contributions to the decade of the brain. Doctrine of multilevel analysis. *American Psychologist, 47*(8), 1019-1028.

11. Cacioppo, J. T., & Decety, J. (2011). Social neuroscience: Challenges and opportunities in the study of complex behavior. *Annals of the New York Academy of Sciences, 1224*, 162-173.

12. Kiecolt-Glaser, J. K., Gouin, J. P., & Hantsoo, L. (2010). Close relationships, inflammation, and health. *Neuroscience and Biobehavioral Reviews, 35*(1), 33-38.

13. Haber, S. N., & Barchas, P. R. (1983). The regulatory effect of social rank on behavior after amphetamine administration. In P. R. Barchas (Ed.), *Social Hierarchies: Essays Toward a Sociophysiological Perspective* (pp. 119-132). Westport, CT: Greenwood Press.

14. Cacioppo, J. T., Amaral, D. G., Blanchard, J. J., Cameron, J. L., Carter, C. S., Crews, D., . . . Quinn, K. J. (2007). Social neuroscience: Progress and implications for mental health. *Perspectives on Psychological Science, 2*(2), 99-123.

15. McGraw, L. A., & Young, L. J. (2010). The prairie vole: An emerging model organism for understanding the social brain. *Trends in Neurosciences, 33*(2), 103-109.

16. Hawkley, L. C., & Cacioppo, J. T. (2003). Loneliness and pathways to disease. *Brain, Behavior, and Immunity, 17 Supplement 1*, S98-105.

17. Hammock, E. A., & Young, L. J. (2004). Functional microsatellite polymorphism associated with divergent social structure in vole species. *Molecular Biology and Evolution, 21*(6), 1057-1063.

18. Wilson, R. S., Krueger, K. R., Arnold, S. E., Schneider, J. A., Kelly, J. F., Barnes, L. L., . . . Bennett, D. A. (2007). Loneliness and risk of Alzheimer disease. *Archives of General Psychiatry, 64*(2), 234-240.

19. Weil, Z. M., Norman, G. J., Barker, J. M., Su, A. J., Nelson, R. J., & Devries, A. C. (2008). Social isolation potentiates cell death and inflammatory responses after global ischemia. *Molecular Psychiatry, 13*(10), 913-915.

20. Ruan, H., & Wu, C. F. (2008). Social interaction-mediated lifespan extension of Drosophila Cu/Zn superoxide dismutase mutants. *Proceedings of the National Academy of Sciences of the United States of America, 105*(21), 7506-7510.

21. Karelina, K., Walton, J. C., Weil, Z. M., Norman, G. J., Nelson, R. J., & Devries, A. C. (2010). Estrous phase alters social behavior in a polygynous but not a monogamous Peromyscus species. *Hormones and Behavior, 58*(2), 193-199.

22. Nonogaki, K., Nozue, K., & Oka, Y. (2007). Social isolation affects the development of obesity and type 2 diabetes in mice. *Endocrinology, 148*(10), 4658-4666.

23. Dronjak, S., Gavrilovic, L., Filipovic, D., & Radojcic, M. B. (2004). Immobilization and cold stress affect sympatho-adrenomedullary system and pituitary-adrenocortical axis of rats exposed to long-term isolation and crowding. *Physiology and Behavior, 81*(3), 409-415.

24. Nation, D. A., Gonzales, J. A., Mendez, A. J., Zaias, J., Szeto, A., Brooks, L. G., . . . McCabe, P. M. (2008). The effect of social environment on markers of vascular oxidative stress and inflammation in the Watanabe heritable hyperlipidemic rabbit. *Psychosomatic Medicine, 70*(3), 269-275.

25. Lyons, D. M., Ha, C. M., & Levine, S. (1995). Social effects and circadian rhythms in squirrel monkey pituitary-adrenal activity. *Hormones and Behavior, 29*(2), 177-190.

26. Cacioppo, J. T., Hawkley, L. C., Norman, G. J., & Berntson, G. G. (2011). Social isolation. *Ann N Y Acad Sci*, *1231*(1), 17-22.